DOCKET NO.: ISIS-5213 PATENT

Application No.: 10/601,242

Office Action Dated: February 22, 2006

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-43. (canceled)

44. (currently amended) A method of treating an organism having a disease characterized by the undesired production of a protein comprising contacting the organism with a compound comprising a plurality of units <u>nucleosides</u> linked by covalent linkages in a sequence that is hybridizable to a complementary nucleic acid encoding the protein, wherein:

said units are selected from nucleosides; and nucleobases:

said nucleosides are selected from α-nucleosides, β-nucleosides including-2'-deoxy-erythro-pentofuranosyl β-nucleosides, and 4'-thionucleosides, and carbocyclic-nucleosides:

said nucleobases are selected from purin 9-yl and pyrimidin 1-yl heterocyclic bases;

said linkages are selected from charged 3'-5' phosphorous, neutral 3'-5' phosphorous, charged 2'-5' phosphorous, neutral 2'-5' phosphorous or non-phosphorous linkages; and

said sequence of linked units <u>nucleosides</u> is divided into at least two regions, wherein:

a first of said regions includes said nucleobases linked by non-phosphorous linkages and nucleobases that are attached to phosphate linkages via non-sugar tethering groups, and nucleosides selected from said α-nucleosides linked by charged and neutral 3'-5' phosphorous linkages, said α-nucleosides linked by charged and neutral 2'-5' phosphorous linkages, said α-nucleosides linked by non-phosphorous linkages, said or said 4'-thionucleosides linked by charged and neutral 3'-5' phosphorous linkages, said 4'-thionucleosides linked by charged and neutral 2'-5' phosphorous linkages, said 4'-thionucleosides linked by non-phosphorous linkages, said carbocyclic-nucleosides linked by charged and neutral 3'-5' phosphorous linkages, said carbocyclic-nucleosides linked by charged and neutral 2'-5' phosphorous

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linkages, said carbocyclic-nucleosides linked by non-phosphorous linkages, said \(\beta\)-nucleosides linked by charged and neutral 2'-5' linkages, and said \(\beta\)-nucleosides linked by non-phosphorous linkages; and

a second of said regions includes said 2'-deoxy-erythro-pentofuranosyl ß-nucleosides linked by charged 3'-5' phosphorous linkages having a negative charge at physiological pH

wherein the compound interferes with production of the protein.

45-68. (canceled)